Comparative effectiveness of Cladribine tablets vs other drugs in relapsing-remitting multiple sclerosis: an approach merging randomized controlled trial with real life data

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Introduction: Cladribine tablets was tested against placebo in randomized controlled trials (RCT).
Objective: To compare the effectiveness of Cladiribine tablets vs other approved drugs in relapsing-remitting multiple sclerosis (RRMS) naïve patients, by matching RCT to observational data.
Methods: Naïve patients from the pivotal trial assessing Cladribine tablets vs placebo (CLARITY) were propensity-score matched to data from the Italian multicenter database i-MuST. This database included 3006 naïve patients diagnosed 2010-2018 in 24 Italian MS centers who started a disease-modifying therapy. The annualized relapse-rate (ARR) over 2 years from treatment start was compared between patients treated with Cladribine tablets and other approved drugs (Interferon, Glatiramer-Acetate, Fingolimod, Natalizumab, Dymethil-fumarate), having the comparisons with placebo as a reference. Treatment effects were estimated by an inverse-probability weighted (IPW) negative-binomial regression model. The treatment effect has been also evaluated according to disease activity (HDA: high disease activity defined as $\geqslant$2 relapses during the year prior to study entry).
Results: From the i-MuST database a total of 1168 patients were treated with Interferon, 402 with Glatiramer-acetate, 113 with Fingolimod, 149 with Natalizumab and 295 with Dymethil-fumarate. Patients' weighted characteristics resulted well balanced between groups. All the tested drugs had an effect vs placebo close to those detected in RCT. Patients treated with Cladribine tablets had a significantly lower ARR as compared with Interferon (RR=0.48;p< 0.001), Glatiramer-Acetate (RR=0.49;p< 0.001) and Dymethil-fumarate (RR=0.6;p=0.011), a comparable ARR with Fingolimod (RR=0.74;p=0.24) and a significantly higher ARR than Natalizumab (RR=2.13;p=0.014). The effect of Cladribine tablets low dose was amplified in HDA patients across all treatments except Fingolimod.
Conclusions: In RRMS patients, Cladribine tablets showed lower ARR compared with matched patients who started another DMT, similar with fingolimod, behind natalizumab. The effect was amplified in the subgroup of HDA patients.
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